

Manoj Gopalakrishnan

Research Summary:

1. Signal transduction in cells

The binding of extra-cellular ligands by cell surface receptors is the first step in signal transduction. Since the number of receptors is often not too large, stochastic concepts are of value in quantitatively understanding this interaction. We have recently developed a self-consistent stochastic formalism for studying reversible ligand association to receptors on a spherical cell surface. The complete time-dependence of the ligand-bound receptor fraction is calculated. Contrary to the commonly accepted view, we find that the effective association rate changes non-monotonically as a function of time, and equals its intrinsic biochemical value at early as well as late times. In an intermediate regime, the well-known Berg-Purcell scaling is satisfied. On the experimental side, this implies the existence of two time-scales for the binding curve. Investigations of the implications of this results for gradient detection in bacterial chemotaxis are currently being pursued.

2. Noise and response in a sensory module

Noise in transduction mechanisms can often interfere with signal perception in sensory systems. A new generating functional formalism has been developed to study the stochastic kinetics of a signaling module with negative feedback (as occurs in many sensory systems). The principal components of such a module are (i) an ion channel that switches randomly between *open* and *closed* conformations, and (ii) a negative feedback effect whereby the incoming ions increases the closing rate of the channel. Analytical results for a single module have been calculated within perturbation theory to second order in feedback strength and to first order in $1/\lambda$, where λ is the intrinsic time-scale of regulation of ion concentration inside the module. Efforts are currently on to generalize the formalism to include several spatially connected modules with diffusion of ions between them.

Publications:

1. Manoj Gopalakrishnan, Peter Borowski, Martin Zapotocky and Frank Jülicher, *Response and fluctuations of a two-state signaling module with feedback*, Phys. Rev. E (2007, in press)

Preprints:

1. Shivam Ghosh, Manoj Gopalakrishnan and Kimberly Forsten-Williams, *Self-consistent stochastic theory of reversible ligand binding to a spherical cell surface*(in preparation).
2. Bindu Govindan, Manoj Gopalakrishnan and Debashish Chowdhury *Enhanced depolymerization of microtubules by MCAK proteins*,(in preparation).

Conference/Workshops Attended:

1. *Modeling infectious diseases: From cell to society*, Institute of Mathematical Sciences, Chennai, India, September 2006.
2. *STATPHYS-KOLKATA VI*, Saha Institute of Nuclear Physics, Kolkata, India, January 2007.

Visits to other Institutes:

1. Institute of Mathematical Sciences, Chennai, India, July 2006.
2. Indian Institute of Technology Kanpur, Kanpur, India, August 2006.

Invited Lectures/Seminars:

1. *Response and fluctuations of a signaling module with negative feedback*, Institute of Mathematical Sciences, Chennai, July 2006.
2. *Theory of ligand binding to cell membrane surfaces*, Department of Physics, IIT Kanpur, August 2006.
3. *Stochastic theory of ligand binding to a spherical surface: How a bacterium lives better and longer by eating less*,*STATPHYS-KOLKATA VI*,Saha Institute of Nuclear Physics, Kolkata, January 2007.

Other Activities:

1. **Teaching:**
'Statistical Mechanics' for HRI graduate students (January-May 2007).
2. **Other lectures:**
 - (a) Two lectures on stochastic processes for VSP students at HRI (May 2006).

- (b) Popular lecture on 'Lipid rafts and cell signaling' at Science Club Meeting, Institute of Mathematical Sciences, Chennai (July 2006).
- (c) HRI internal symposium lecture: *How a bacterium can survive better by eating less*(March 2007).

3. Mentoring students:

- (a) I supervised the research projects of these students in the Condensed Matter Visiting Students Program (VSP).
 - i. Shivam Ghosh, St. Stephen's College, Delhi(May-June 2006)
 - ii. Abhishek Mukhopadhyay, IIT Kanpur(May-June 2006)
 - iii. Arnab Banerjee, Jadavpur University(September 2006)
 - iv. Jonathan Dawson, Allahabad Agricultural Institute-DU(November-December 2006)
- (b) Supervised the term paper/course project in Statistical Mechanics (M.Sc 2nd year, IIT Kanpur) of Abhishek Mukhopadhyay (August-December 2006), Title: *Effect of solution receptors in dissociation of ligands bound to surface receptors.*